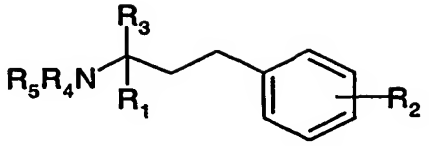
CLAIMS

1. A compound of formula I



I

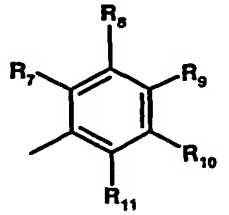
wherein

R_1 is C_{1-6} alkyl optionally substituted by OH, C_{1-2} alkoxy or 1 to 6 fluorine atoms; C_{2-6}alkenyl; or C_{2-6}alkynyl;

R_2 is R_2' or R_2"

wherein R_2' is X_1, -O-X_1, -CO-X_1, -CH(OH)-X_1, –C(NOR_6)-X_1, -S-X_1, -SO-X_1, -SO_2-X_1 or –N(C_{1-6}alkyl)-X_1 wherein X_1 is C_{3-8} alkyl substituted by 1 to 17 fluorine atoms and optionally interrupted in the carbon chain by one or more O, C=O, CH-OH or C=NOR_6 and/or one carbon-carbon double or triple bond; pentyl substituted by C_{1-3}alkyl and optionally interrupted in the carbon chain by one or more O, C=O, CH-OH or C=NOR_6 and/or one carbon-carbon double or triple bond; C_{2-8}alkyl-C_{3-6}cycloalkyl wherein the C_{2-8}alkyl moiety is optionally interrupted in the carbon chain by one or more O, C=O, CH-OH or C=NOR_6 and/or one carbon-carbon double or triple bond, and the C_{3-6}cycloalkyl and/or the C_{2-8}alkyl is substituted by 1 to 17 fluorine atoms; and each of R_6, independently, is H, C_{1-4} alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl or benzyl; and

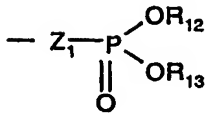
and wherein R_2" is X-CH_2-CH_2-R attached in position para, wherein X is O; CH_2; or C=O; and R is a residue of formula (b)



(b)

wherein each of R_7 to R_{11}, independently, is H; Cl; Br; F; CN; CF_3; OCF_3; $OCHF_2$; C_{1-6}alkyl; C_{1-6}alkoxy; C_{3-6}cycloalkyl; C_{3-6}cycloalkoxy; acyl; or optionally substituted phenyl; or R_9 and R_{10} form together 3,4-[-O(CH_2)$_r$O-] wherein r is 1 or 2; or (R_7 and R_8) or (R_8 and R_9) together with the carbon atoms to which they are attached, form a fused cyclic or heterocyclic ring and the remaining R_9 to R_{11} or R_7 and R_{10} and R_{11}, respectively, are as defined above; or R is α- or β-naphthyl optionally substituted by one to 5 substituents as defined above for R_7 to R_{11};

R_3 is $Z\text{-}X_2$ wherein Z is CH_2, CHF or CF_2 or CHMe and X_2 is OH or a residue of formula (a)



(a)

wherein Z_1 is a direct bond, CH_2, CHF, CF_2 or O, and each of R_{12} and R_{13}, independently, is H or C_{1-4} alkyl optionally substituted by 1, 2 or 3 halogen atoms; and each of R_4 and R_5, independently, is H, C_{1-4}alkyl optionally substituted by 1, 2 or 3 halogen atoms, or acyl

in free form or in salt form.

2. A compound according to claim 1 wherein R_2 is R_2' which is X_1, $-O-X_1$, $-CO-X_1$, $-CH(OH)-X_1$ or $-C(NOR_6)-X_1$.

3. A compound according to claim 2 wherein R_2' is a residue of formula (c)

$$-Y-(CH_2)_n-(CF_2)_m-CH_pF_q \qquad (c)$$

wherein

Y is a direct bond, O, CO, CHOH or $C{=}NOR_6$ wherein R_6 is as defined above;

n is 0, 1,2, 3, 4 or 5;

m is 0, 1, 2, 3, 4, 5 or 6, provided that the sum of n+m is 3-8;

each of p and q, independently, is 0, 1, 2 or 3,

the chain $(CH_2)_n-(CF_2)_m-CH_pF_q$ being optionally interrupted by one carbon-carbon double or triple bond, one CO or one or two oxygen atoms.

4. A compound according to claim 2 or 3 wherein R_2' is selected from the group consisting of

$-Y-C_nF_{2n+1}$ wherein n=3-8 and Y is CH_2, O or C=O;

$-Y-CH_2C_nF_{2n+1}$ wherein n=1-7and Y is CH_2, O or C=O;

$-Y-CH_2CH_2C_nF_{2n+1}$ wherein n=1-6 and Y is CH_2, O or C=O;

$-Y-CH_2CH_2CH_2\ C_nF_{2n+1}$ wherein n=1-5 and Y is CH_2, O or C=O;

$-Y-(CH_2)_nF$ wherein n=1-7 and Y is CH_2, O or C=O;

$-Y-(CH_2)_nCF_3$ wherein n=1-6 and Y is CH_2, O or C=O;

$-Y-(CH_2)_nCF_2CH_3$ wherein n=1-4 and Y is CH_2, O or C=O;

$-Y-(CH_2)_n(CF_2)_mCHF_2$ wherein n=0-3, m=1-6, n+m = 3-7 and Y is CH_2, O or C=O; and

$-Y-(CH_2)_nC(O)CF_3$ wherein n=1-5 and Y is CH_2, O or C=O.

5. A compound according to claim 1 wherein R_2 is R_2".

6. A compound according to claim 5 wherein R is β-naphthyl optionally substituted by one to 5 substituents or R is a residue of formula (b), wherein one or two of the residues R_7 to R_{11} independently, is Cl, Br, F, CF_3, OCF_3, C_{1-6}alkyl, C_{1-6}alkoxy, or optionally substituted phenyl, and the other residues R_7 to R_{11} are H, and/or

7. A compound according to any one of claims 1 to 6 or a pharmaceutically acceptable salt thereof for use as a pharmaceutical and for use in the preparation of a medicament.

8. A pharmaceutical composition comprising a compound according to any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof in association with a pharmaceutically acceptable diluent or carrier therefor.

9. A pharmaceutical combination comprising a compound according to any one of claims 1 to 6, in free form or in pharmaceutically acceptable salt form, and at least one co-agent.

10. A method for preventing or treating disorders or diseases mediated by lymphocytes,and for preventing or treating acute or chronic transplant rejection or T-cell mediated inflammatory or autoimmune diseases in a subject comprising administering to the subject in need thereof an effective amount of a compound according to any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof.